Reviewer’s report

Title: Design effect in multicenter studies: gain or loss of power?

Version: 1 Date: 21 August 2008

Reviewer: Sally Kerry

Reviewer's report:

Major Compulsory revisions
The calculation of the design effect assumes there are numerous centres. Some trials or studies may have few centres. It needs to be clarified how sensitive the statistic S is to this assumption and there should be a discussion of when the results apply.

The paper appears to be correct as far as it goes but I feel has limited usefulness in its present form.

Minor essential revisions
1. The abstract refers to the statistic S, which is only defined in the paper. Neither is it clear what is meant by 'group proportions' in the sentence to describe S.

The English is good and grammatical but there are a few things which could be more clearly expressed.
2. Background 'treatment/group' should be 'treatment or group'
3. page 7 last para I found this confusing. I wasn't sure what 'group proportions' and 'balanced proportions' were

Discretionary revisions
1. the conclusions that a centre effect should be taken into account when analysing data from a multicentre study is a reasonable recomendation but one that could be made in the absence of this paper. What teh authors have attempted to add is a measure of the effect of clustering. However, the methods of analysis proposed give equal weight to each subject, a strategy that is known to be inefficient where there is a large degree of imbalance between the clusters sizes. Hence the authors may be overestimating the problem when subjects are individually randomised. More discussion should be given to different methods of analysis.

2. There is no discussion of whether the examples shown are similar to those likely to arise in practice. A situation where each cluster has the same number of individually randomised subjects but has strong heterogeneity as desmonstrated in Table 2 seems unlikely to occur in practice.

3. The examples should not be restricted to those where the clusters are the same size. The situations where there is great imbalance in total between
centres occurs, either because some centres are more enthusiastic recruiters than others or because they have more patients is quite common but has not been included here.

4. The greatest value in estimating the design effect is when planning the study. Some degree of imbalance is unavoidable but other sources can be controlled. However it is difficult to use the formulae provided in advance of the study or to estimate its likely value from this paper.

5. Other authors has written about the effect of imbalance on the design effect in cluster randomised trials but these papers have not been referenced or discussed.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

The only possible competing interest is publishing in the same field. However I have no plans to submit any paper for publication on the topic of imbalance and clustering.